## P49

### Pagetoid Dyskeratosis and Pachydermodactyly-Mechanically induced Dermatoses ?

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Introduction: Pachydermodactyly is a rare benign form of digital fibromatosis, preferrably seen in adolescent males. The disease is characterized by a painless soft tissue swelling of the proximal interphalangeal (PIP) joints of the second to the fifth finger.
Pagetoid dyskeratosis is an incidental finding in a variety of lesions of the skin and squamous mucosa, presenting as a brownish maculae, typically found in areas of the skin, which are mechanically stressed such as intertriginous areas, buttocks and genitals. We herein report the first patient, who simultaneously presented these two rare diseases in the area of the hands.
Patient/methods: We report a case of a 14-year-old boy, who was sent to our department because of a brownish pigmentation of digit I-III and IV of the left hand and digit IV of the right hand, which were evolving four months. Additionally he presented a swelling of the lateral and dorsal regions of the metacarpophalangeal joints of digit III and IV of both hands since six months. He did not show any inflammatory signs or symptoms. The patient's history did not reveal any repetitive trauma, contact with chemicals and dyes or substance abuse.
Results: Laboratory studies showed no abnormalities, namely antinuclear antibodies, anti-doubled-stranded DNA, and rheumatic factor were found negative. X-ray exams only revealed augmentation of soft parts in the PIP.
Dermoscopic examination suggested that the lesions could be pigment lesions. A biopsy specimen of the fingertip showed no melanocytes, pigment- or hemosiderin deposits and no tumorous alterations. Pale pagetoid cells within the epidermis, some of which were dyskeratotic, led to the diagnosis of pagetoid dyskeratosis.
Discussion: Some authors postulate that pagetoid dyskeratosis is caused by trauma and friction. It is often present in areas which are subject to friction or moisture from occlusion. Pachydermodactyly is oft en associated with mechanical stress due to repetitive movements.
The observation of the two rare conditions in one patient, support the idea that both are induced by repetitive microtraumatic actions. To our knowledge we herein present a new case of pagetoid dyskeratosis of the hand and first in combination with pachydermodactyly.

## P50

### Increased expression of heat shock protein 90 in keratinocytes and mast cells in psoriasis

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Psoriasis is a chronic inflammatory skin disease and various stress factors mediate initiation and perpetuation of skin inflammation. Heat shock protein (HSP) 90 is a protein that acts as chaperone to protect cells from environmental stress signals and also has many roles in cell survival, cytokine signaling, such as IL-17 receptor signaling, as well as adaptive and innate immune responses. To elucidate the role of HSP90 in psoriasis, we assessed HSP90 expression and found that HSP90α, the inducible isoform of HSP90, was significantly upregulated in epidermal keratinocytes and mast cells of lesional psoriatic skin and downregulated following ustekinumab therapy. In vitro heat stress induced HSP90α mRNA expression and protein secretion in both human keratinocyte cell line HaCaT and human cord blood-derived mast cells (CB-MCs). HSP90α mRNA was upregulated by IL-6, IL-17, and IL-22 and HSP90α protein secretion was increased by TNF-α in HaCaT cells. HSP90α mRNA upregulat ion and protein production were induced by stem cell factor in CB-MCs. Finally, inhibition of HSP90 reduces proliferation in HaCaT cells and survival in CB-MCs. Our findings suggest that HSP90 from keratinocytes and mast cells is a key regulator in both the induction and maintenance of psoratic inflammation and provide a rationale for a novel therapeutic approach with HSP90 inhibitors.

## P51

### Expression of IL-17 in acute generalized exanthematous pustulosis and generalized pustular psoriasis

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Introduction & objectives: Acute generalized exanthematous pustulosis (AGEP) is a rare pustular disorder, mostly attributed to drugs, and characterized by sterile pustules, fever, and neutrophilia. CXCL8 producing drug-specific T lymphocytes are involved in the pathogenesis of AGEP. IL-17 is a pro-inflammatory cytokine and involved in various neutrophil-related autoimmune diseases. However, little is known about the role of IL-17 in AGEP. In this study we investigated the expression of IL-17 in AGEP in comparison to generalized pustular psoriasis (GPP) and normal skin.
Materials & Methods: Skin biopsy specimens were obtained from patients with AGEP (n=8), GPP (n=7) and from normal controls (n=8). IL-17 mRNA and protein expression were evaluated by in situ hybridization and immunohistochemistry. IL-17 positive cells were counted in the epidermis, upper dermis,

and deep dermis, respectively. Furthermore, double immunohistochemistry and double immunofluorescence were performed to characterize the IL-17 producing cells, using the following markers: CD3, CD66b, CD68, and mast cell tryptase.
Results: In AGEP and GPP, IL-17 positive cells were significantly increased compared to normal skin in pustules, epidermis, upper dermis, and deep dermis. No significant difference in the number of IL-17 positive cells was found between AGEP and GPP. IL-17 was mainly expressed by mast cells, neutrophils, macrophages and only by a minority of T lymphocytes.
Conclusions: Innate immune cells such as macrophages, neutrophils and mast cells are important cellular sources of IL-17 in AGEP and GPP, suggesting that IL-17, promoting neutrophil recruitment and survival, may contribute to the pathogenesis of these neutrophil-related pustular diseases.

**P52**

**Hydroxychloroquine induced hyperpigmentation**

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Antimalarial medications are widely used to treat different autoimmune diseases. Although pigmentation of the skin is a well-known side effect of cholorquine, it is rarely reported for hydroxychloroquine. We report on a 49-year old female, diagnosed with rheumatoid factor positive, anti-CCP antibody negative rheumatoid arthritis. She presented with a widespread grayish-brown macular pigmentation of the skin after intake of 400mg hydroxychloroquine daily over a period of 13 months. Face, neck, shoulders, upper back, arms and hands were affected, leaving the oral mucosa and nails spared. There was neither a history of preceding inflammation nor of any medication with other drugs likely to cause hyperpigmentation. Skin biopsy revealed deposits of granular brown pigments in the upper corium identified as melanin.
In the absence of other possible conditions causing localized or generalized pigmentation in our patient, hydroxychloroquine was the most probable cause , in this case affecting the skin much more extensively than previously reported. Accumulation of melanin as shown here is one of the four main pathogenetic mechanisms responsible for drug-induced hyper-pigmentatons; hydroxychloroquine has an affinity for the melanin pigment in the skin. Although mucosal involvement is described in two cases, the distribution pattern in our patient is consistent with sun-exposed areas. Phototoxic and photoallergic reactions due to hydroxychloroquine have been observed, supporting the idea of a drug-triggered photo-induced pigmentation with granular melanin depositions.
In conclusion, when prescribing hydroxychloroquine, the rare possibility of skin pigmentation should be taken into consideration, particularly because this effect appears to be at least partially permanent. Besides the suggested regular ophthalmological examinations, skin checks should be performed; drug discontinuation should be evaluated if pigmentation appears. As sun radiati on seems to be involved in the pathogenesis, protective measures should be recommended.

**P53**

**Lymphoplasmacytic plaque - a recently recognized lymphoproliferative process - presentation of clinico-pathological features in four childhood and adult cases**

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Lymphoplasmacytic plaque (LPP) is a recently recognized cutaneous lymphoproliferative process. It affects almost exclusively children and is characetrized by a solitary, long standing violaceous to brown plaque usually arising on the lower leg. Histologically, a dense lymphocytic infiltrate with plasma cells and a variable histocytic component is present. So far, less than ten cases have been documented in the literature. We present 4 cases of LPP occuring in two children (3 and 13-years-old girls) and two adults (a 61-year-old and a 64-year-old woman).
In one girl and one woman the erythemato-squamous plaque was located on the upper arms and measured up to 5 x 2 cm, whereas in the other two patients the lesions were located on the lower legs. Histologically, dense infiltrates of small lymphocytes, plasma cells and histiocytes forming granulomas in two of four cases were found. No infectious agent (spirochetes, mycobacteria, fungi and parasites) were identified b y special stains, immunohistochemistry or by PCR. The plasma cells were polyclonal as shown by in situ hybridization. No clonal T- or B-cell population was present as demonstrated by PCR. In one patient the lesion was completely excised and no relapse was observed. Two patients experienced persistence of LPP after incisional biopsy. In one patient LPP was treated by cryosurgery and photodynamic therapy resulting in partial remission, but the lesion showed regrowth almost to its original size within a few weeks.
Our series of four cases expands the age range of patients with LPP, demonstrating that LPP not only arises in children, but affects adults as well. Moreover, LPP is not restricted to the lower legs, but may also involves the arms. The persistence after incisional biopsy and the lack of response to various therapies corroborates previous observations reported in the literature. Dermatologists and dermatopathologists should be aware of this rare, but therapy reluctant pseudolymphomatous process of yet unknown etiology.